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TITLE:

Wound Status Early Outcome Sensor and 3D Construct Development

PRINCIPAL INVESTIGATOR:
Laura E. Edsberg, Ph.D.

CONTRACTING ORGANIZATION:
Daemen College
Amherst, NY 14226

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14. ABSTRACT

Early identification of the specific proteins, which indicate delayed healing are critical to long-term success of the patient and the development of new treatments. It is the objective of this research to correlate changes in the proteome of wounds with clinical outcome and develop technology to sense these changes. Protein Imprinted Xerogels with Integrated Emission Sites (PIXIES) and porous polymer photonic bandgap (PBG) structures are being integrated to sense the wound bed in real time. Flexible bandgap structures and micro-concave shaped gratings have been developed to conform to the curved anatomy of the wound bed.

15. SUBJECT TERMS

Chronic wound, proteome, porous photonic bandgap, healing, real time sensing

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INTRODUCTION

Early identification of the specific proteins, which indicate delayed healing are critical to long-term success of the patient and the development of new treatments. It is our hypothesis that real time sensing of the wound proteome can be used to predict wound outcome, resulting in tailored treatment that improve acute and chronic wound healing. The focus of this proposal is to correlate protein targets and wound outcome and develop a technology that can sense the microenvironment in acute and chronic wounds.

BODY

Statement of Work

<u>Technical Objective 1:</u>

Develop technologies for sensing multiple proteins in the wound microenvironment, in real time.

Subtask 1.1 Develop xerogel-based elements.

Subtask 1.2 Develop PBG-based sensor platforms.

Subtask 1.3 Sensor design and evaluations using wound fluids

<u>Technical Objective 2:</u>

Test the suitability of our technology for the detection of multiple proteins from acute and chronic wounds in vitro and in vivo, and correlate results with clinical outcomes.

Subtask 2.1 Collect fluid from subjects with pressure ulcers.

Subtask 2.2 Collect samples from wounds in porcine model

Subtask 2.3 Proteomic analysis of wound fluid

Technical Objective 1:

Subtask 1.1 Develop xerogel-based elements. **Completed.**

Subtask 1.2 Develop PBG-based sensor platforms. **Completed**

Subtask 1.3 Sensor design and evaluations using wound fluids

Task is in progress. Delayed enrollment of human subjects has delayed the completion of this task. Enrollment is ongoing an additional site has been added to increase enrollment.

Technical Objective 2:

Subtask 2.1 Collect fluid from subjects with pressure ulcers.

Enrollment of human subjects is ongoing. Inclusion criteria were modified to potentially increase rate of enrollment. Amendment to protocol was approved by all local IRB's and USAMRMC, ORP, and HRPO. Also, an additional site has been added to potentially increase the rate of enrollment. The University at Buffalo and Daemen College IRBs have reviewed our additional site and approved. We have submitted the additional site to the (USAMRMC), Office of Research Protections, Human Research Protection Office and Daemen College IRB for review. No subjects will be enrolled at this new site until approval is received from the (USAMRMC), Office of Research Protections, Human Research Protection Office. The addition of this and the 1-year NCE will allow us time to both enroll subjects, collect samples, and analyze data.

Subtask 2.2 Collect samples from wounds in porcine model

In vivo models for normal and healing-impaired (chronic wounds) are in place; the healing impaired model (diabetic pig) has been approved by University at Buffalo IACUC Office but has not yet been tested experimentally.

Subtask 2.3 Proteomic analysis of wound fluid

The task has been delayed due to slow human subject enrollment. This task will begin when sufficient samples have been collected to allow analysis.

The current research is novel with respect to current published research in the field. There are no published studies utilizing PIXIES to evaluate the biochemistry of wounds during healing. Differential protein expression between healing and non-healing pressure ulcers has identified proteins, which may serve as indicators of wound healing. It is anticipated that some of the proteins identified will be significant with regard to our understanding of the healing of chronic wounds, as well as serving as potential biomarkers of healing. These biomarkers will serve as the basis of the array for the technology for sensing the wound bed in real time.

KEY RESEARCH ACCOMPLISHMENTS

- Xerogel-basesd sensor elements developed.
- PBG-based sensor platforms developed.
- PIXIES platform developed and verified for cytokine detection of both *in vitro* and *in vivo* (thermally injured normoglycemic pig) wound fluids.
- Normal and healing impaired animal models are approved and ready for use in device testing.
- Animal model for impaired healing approved.

REPORTABLE OUTCOMES

- Ka Yi Yung, Huina Xu, Ke Liu, Greggory J Martinez, Frank V. Bright, Michael R Detty, and Alexander N. Cartwright, "Hybrid Oxygen-responsive Reflective Bragg Grating Platforms", Analytical Chemistry (Accepted)

- Ke Liu, Huina Xu, Haifeng Hu, Qiaoqiang Gan, and Alexander N. Cartwright, "One-step Fabrication of Graded Rainbow-colored Holographic Photopolymer Reflection Gratings", Advanced Material (Under Review)

- Ke Liu, Huina Xu, Qiaoqiang Gan, and Alexander N. Cartwright, "One-step Holographic Lithography Fabrication of a Rainbow-colored Photonic Bandgap Structure", IEEE Photonics 2011 Conference, Oct. 2011, Arlington, Virginia

- Huina Xu, Ke Liu, Qiaoqiang Gan, and Alexander N. Cartwright, "Flexible Porous Polymer Photonic Bandgap Structures for Chemical and Biomedical Sensing", IEEE Photonics 2011 Conference, Oct. 2011, Arlington, Virginia.

- Ke Liu, Huina Xu, Qiaoqiang Gan, and Alexander N. Cartwright, "Polymeric Concave Bragg Reflectors Fabricated using Optical Lithography", Materials Research Society, Nov. 2011, Boston, Massachusetts.

CONCLUSION

The development of a technology to real-time sense the proteome of a wound bed is ongoing. The fabrication of flexible sensors is significant in the development of a point of care sensing device. The evaluation of wounds in a porcine model allows refinement of the system while the future enrollment of human subjects will allow confirmation for the relevant proteins for the sensing platform for this novel technology. Ultimately this work may allow the development of personalized wound care based on the real-time characteristics of the wound.